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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/771,382	01/25/2001	Ian Richard Anselm Peak	8795-24 U1	6450

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/771,382	Applicant(s) PEAK ET AL.	
	Examin r Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears n the c ver sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-36* is/are pending in the application.

4a) Of the above claim(s) *26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-32,35 and 36* is/are rejected.

7)☒ Claim(s) *33 and 34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *22* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 30, 2003 has been entered. Applicant's amendment and response is acknowledged. Claim 25 has been amended. Claim 28 has been amended. Claims 35 and 36 have been added. Upon further consideration and review claim 29 will be examined because claim 29 recites SEQ ID Nos that are species of the claimed genus of polypeptides as set forth in SEQ ID NO:11. Claims 33 and 34 will also be examined because SEQ ID NO: 23 and SEQ ID NO: 35 represent two species of the claimed genus of polypeptides as claimed in SEQ ID NO: 11.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejection Maintained

3. The rejection under 35 U.S.C. 112, first paragraph is maintained for claims 28, 30 and newly submitted claims 35 and 36 for the reasons set forth pages 4-7, paragraph 5 of the previous Office Action.

The rejection was on the grounds that the claims are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification broadly describes as a part of the invention polypeptides that are variants or fragments of SEQ ID No. 11. The specification discloses the claimed invention also contemplates fragments, derivatives and variants (such as allelic variants) of the exemplified proteins (page 13). The specification states " that amino acids can be deleted from any of the C1-5 sequences set forth in Figure 1, while not all non-conserved amino acids in the V1-4 regions need be deleted in order to reduce strain-specific immunogenicity and isolated proteins of the invention may include fragments of the C1-5 and V1-4 regions" (page 13). The specification also states " that a "fragment" includes an amino acid sequence that constitutes less than 100%, but at least 20%, preferably 50%, more preferably at least 80% or even more preferably at least 90% of said C1, C2, C3 C4 or C5 regions". Applicant has broadly described the invention as embracing any substitution, insertion or deletion change of amino acids throughout the length of the polypeptide sequence. Variants or fragments of SEQ ID No: 11 correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 U.S.C. 112, first, paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of allelic variants or fragments of SEQ ID NO: 11 that are encompassed by the polypeptides of the invention regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, the full breadth of the claim (or none of the sequences encompassed by the claim, i.e. variants or fragments of SEQ ID No: 11) does not meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant urges that claim 25 had been cancelled and its recitations have been incorporated into claim 28. Applicant urges that the Examiner's position is that the unrestricted open-ended language of claim 28 prior to the present Amendment and the broad scope of the invention was not adequately described in the specification. Applicant urges that claim 28 has been amended to indicate that the isolated protein still comprises at least one conserved region of SEQ ID NO:11 but recites that the conserved region consists of at least five recited amino acid residue groups. Applicant also provides that the isolated protein has at least one variable region and that the variable region or regions consist of an amino acid sequence selected from four specific amino acid groups. Applicant urges that claim 28 still encompasses a variety of possible amino acid substitutions at residues marked "X" in SEQ ID NO:11, however the sequence listings specifies that each non-conserved residue can be any residues present in the corresponding molecule of SEQ ID Nos:1-10 since SEQ ID NO: 11 is a consensus sequence listing. Applicant urges that the specification provides adequate written description and enablement and that they were possession of the invention as of the filing date.

Applicant's arguments filed October 25, 2002 have been fully considered but they are not persuasive. It is the Examiner's position that there is nothing of the record to that the specification is enabled for the full scope of the claims and therefore does not meet the written description requirement as set forth in 35 U.S.C. 112, first paragraph. Applicant has not shown written description for an allelic variants having at least 80% to 90% amino acid identity to the isolated protein of claim 28. The specification states that

"isolated proteins of the invention may include fragments of the C1-C5 (conserved regions) and fragments of V1-V4 (variable regions) (page 13). The specification also discloses that the "a fragment" includes an amino acid sequence that constitutes less than 100%, but at least 20% of conserved regions C1-C5 (page 13). Therefore, the claimed invention includes fragments and allelic variants of the conserved regions of the claimed protein. The claims broadly teach polypeptides that have 80% to 90% identity to the polypeptides of SEQ ID NO:11 which includes substitutions, insertion or deletions and therefore any amino acid is being claimed. The specification teaches no specific location for where the deletion, substitution or insertion or any combination thereof can be (or some equivalent) is recited. If 10% to 20% of the amino acids are substituted, deleted or inserted the resulting polypeptide could result in a polypeptide not taught nor enabled by the specification. Further, it is unclear how to define the isolated polypeptide since the metes and bounds of the polypeptides are not known. There is no guidance as to what amino acids may not be changed without causing a detrimental effect to the polypeptide being claimed.

While the use of mutagenesis techniques are known in the art, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the polypeptide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in any polypeptide and the result of such modifications is unpredictable based on the instant disclosure. The skilled artisan would require guidance to in order to make and use the claimed isolated proteins commensurate in scope with the claims. Therefore,

only SEQ ID NO: 11, SEQ ID NO:23 (species of SEQ ID NO:11) and SEQ ID NO: 35 (species of SEQ Id NO:11) but not the full breadth of the claim (i.e. allelic variants of SEQ ID NO:11) meets the written description provision of 35 USC 112, first paragraph.

4. The rejection under 35 U.S.C. 102(e), is maintained for claims 28-32 and newly submitted claims 35 and 36 for the reasons set forth on pages 8-9, paragraph 6 of the previous Office Action.

The rejection was on the grounds that Peak et al teach an isolated polypeptide from *Neisseria meningitidis* and pharmaceutical compositions containing the polypeptide (see the Abstract). Peak et al teach pharmaceutical compositions for treating patients against *N. meningitidis* infections, which comprises polypeptides, fragments, variants or derivatives and a pharmaceutically acceptable carrier (column 16, lines 6-64). Peak et al teach that the compositions of the invention may be used as therapeutic or prophylactic vaccines (column 16, lines 65-66). The claimed isolated protein comprising at least twelve contiguous amino acids of a conserved region of SEQ ID NO: 11 (i.e. amino acid residues 109-120) is the same as amino acid residues 105-116 of SEQ ID NO: 5 of the prior art (see attached sequence alignment). The protein, pharmaceutical composition and vaccine of Peak et al appear to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein, pharmaceutical composition and vaccine with the protein, pharmaceutical composition and vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein, pharmaceutical composition and vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed protein, pharmaceutical composition and vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that the first issue to address is that if Peak (*U.S. Patent No. 6, 197, 312)* is an appropriate reference under 35 U.S.C. 102(e) since two of the three inventors of the Peak Patent are co-inventors on the present application. Applicant urges that although *N. meningitides* is a common starting material in the Peak Patent

and the present invention, the Peak Patent does not identify the particular conserved and variable regions of SEQ ID NO:11 as now claimed in the present application. Applicant urges that the variable regions of the present application cannot be reasonably considered to have been disclosed in the Peak Patent. Applicant urges that the Examiner refers to a general disclosure in the Peak Patent relating to deletion mutants and there is no explicit disclosure of a mutant having at least one fewer variable region as disclosed in claim 28 compared to the wild-type NhhA polypeptide disclosed in Peak.

Applicant's arguments filed June 30, 2003 have been fully considered but they are not persuasive. It is the Examiner's position that there is nothing of the record to show why the isolated polypeptide and composition comprising the isolated polypeptide is not the same as claimed polypeptide and composition. Peak et al teach an isolated polypeptide from *Neisseria meningitidis* and pharmaceutical compositions containing the polypeptide (see the Abstract). Peak et al teach pharmaceutical compositions for treating patients against *N. meningitidis* infections, which comprises polypeptides, fragments, variants or derivatives and a pharmaceutically acceptable carrier (column 16, lines 6-64). Peak et al teach an isolated polypeptide (SEQ ID NO: 17) which has the amino acid sequence of SEQ ID NO:34. (columns 83-84 to columns 85-86) which meets the limitations of the claims (in particular claim 29).

As to Applicant's arguments regarding Peak et al as being not appropriate

102(e) reference, 35 U.S.C. 102(e) states:

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Peak et al is an appropriate reference under 35 U.S.C. 102(e) because the Peak et al reference is a U.S. Patent granted on an application for patent by another in the United States. The inventors on Peak et al are Ian Peak, Michael Jennings and E. Richard Moxon. The inventors on this patent application are Ian Peak and Michael Jennings. The inventors of the instant application and the Peak et al (issued *U.S. Patent No. 6,197, 312 B1*, filed August 19, 1999) are different. There is nothing on the record to show that the isolated polypeptide of the prior art is not the same as the claimed invention. Therefore, the teachings of Peak et al anticipates that claimed invention.

New Grounds of Rejection

Claim Objections

5. Claim 33 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

6. Claim 34 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 28, 30-32 and 35-36 are rejected under 35 U.S.C. 102(a) as anticipated by Masignani et al *(WO 99/36544, published July 1999).*

Claims 28, 30-32 and 35-36 are drawn to an isolated protein comprising at least one conserved conserved region of SEQ ID NO:11 that consists of an amino acid sequence selected from the group consisting of

(i) residues 1 to 50 of SEQ ID NO: 11;

(ii) residues 109 to 120 of SEQ ID NO: 11;

(iii) residues 135 to 198 of SEQ ID NO: 11;

(iv) residues 221 to 239 of SEQ ID NO: 11 and

residues 249 to 604 of SEQ ID NO:11 and at least one variable region of SEQ ID NO:11 that consists of:

(a) residues 51 to 108 of SEQ ID NO: 11;

(b) residues 121 to 134 of SEQ ID NO: 11;

(c) residues 199 to 220 of SEQ ID NO: 11; and

(d) residues 240 to 248 of SEQ ID NO: 11;

wherein the isolated protein has at least one fewer variable region than a wild-type NhhA polypeptide and wherein upon administration to a mammal the protein elicits an immune response against one or more strain of *N. meningitidis*.

Masignani et al teach an isolated polypeptide from *Neisseria meningitidis* and immunogenic pharmaceutical compositions containing the polypeptide (see the Abstract). The claimed isolated protein comprising at least one a conserved region of SEQ ID NO: 11 that consists of (amino acid residues 221-239 of SEQ ID NO:11) is the same as amino acid residues 189-210 of SEQ ID NO: 4 of the prior art (page 62) and at least one variable region of SEQ ID NO:11 that consists of an amino acid sequence selected from the group consisting of (amino acid residues 240 to 248 of SEQ ID NO:11 which is the same as amino acid residues 162-170 of SEQ ID NO:4). The protein and immunogenic composition of Peak et al appear to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's protein and immunogenic composition with the immunogenic composition and vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein and immunogenic composition and vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed protein and immunogenic composition). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

8. No claims allowed.

Conclusion

9. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
October 26, 2003

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